Synopsis

"Synthesis of Novel Iminothaizolidinones Derivatives, Characterization and its biological activities"

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Chemistry

Submitted By

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SYNOPSIS

"Synthesis of Novel Iminothaizolidinones Derivatives, Characterization and its Biological Activities"

Introduction:

Thiazolidinones are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds containing sulfur and nitrogen in a five member ring. A lot of research work on thiazolidinones has been done in the past. The thiazolidinone nucleus is also known as "wonder nucleus" because it gives out different derivatives with all different types of biological activities[1]. Thiazolidin-4-one derivatives are known to exhibit diverse bioactivities such as anti-convulsant [2], anti-diarrheal [3], anti-platelet activating factor[4], anti-histaminic[5], anti-microbial[6], anti-diabetic[7], cycloxygenase inhibitory[8], Ca2+channel blocker[9], PAFantagonist[10], cardioprotective[11], anti-ischemic[12], anticancer[13], anti-HIV[14], non-peptide thrombin receptor antagonist[15] and tumor necrosis factor-α antagonist activities[16]. The treatment of infectious disease always remains an important and challenging problem. A search of novel antimicrobial agents is a field of current and growing research interest because of a combination of factors including emerging infectious diseases and the increasing number of multi-drug resistant microbial pathogens with particular relevance for gram positive bacteria. The therapeutic problem has achieved increasing importance in hospitalized patients, in immune suppressed patients with AIDS or undergoing anticancer therapy and organ transplants, because of emergence of old and new antibiotic resistance created in the last few decades. Therefore, there is a substantial medical need for new classes of antibacterial agents.

A potential approach to overcome the resistance problem is to design innovative agents with a different mode of action so that no cross resistance with the present therapeuticals can occur. Recently, "Linezolid'', a totally synthetic molecule of the oxazolidinone class, has been approved for human use and consistent with its activity against resistant gram positive organism, appeared to have a unique mechanism of antibacterial activity[17-19] Peptidoglycan is an essential component of the cell wall of both gram-positive and gram-negative bacteria. Thiazolidin-4-ones

have been reported as novel inhibitors of the bacterial enzyme Mur B which is precursor acting during the biosynthesis of peptidoglycan[20].

Considering the above facts and in continuation of our ongoing research program in the field of synthesis and antimicrobial activity of Iminothiazolidinone compounds and its biological evaluation. We further exploring the work for "Synthesis of Novel Iminothaizolidinones Derivatives, Characterization and its Biological Activities"

Review of Literature and Development in the subject:

Fluoro and trifluoromethylated compounds are of particular interest as the strong electron-withdrawing effect of F and CF3 groups contributes to a number of biologically important molecular properties. Some of the most well known fluorine-containing drugs with antibacterial activity are the fluoroquinolones. The isosteric substitution of hydrogen by fluorine in organofluorines compounds may increase the lipophilicity and thus enhance the rate of cell penetration, which is a very important feature in drug delivery, both referring to prokaryotic, Gram-negative bacteria as well as eukaryotic cells. The higher polarizability due to the C-F bond may give rise to new possibilities for binding to the receptor. Fluorine substitution can also influence pharmacokinetic and pharmacodynamic properties of the molecule [21]. Linezolid, a totally synthetic molecule of the oxazolidinone class also possesses Fluorine atom in its structure. Patil.et.al reported the fluorinated Iminothiazolidinone derivatives as potential antimicrobial agents[22]

Objectives of Research:

Thiazolidin-4-one derivatives are known to exhibit diverse bioactivities such as anti-convulsant, anti-diarrheal, anti-platelet activating factor, anti-histaminic, anti-microbial, anti-diabetic, cycloxygenase inhibitory, Ca2+ channel blocker, PAF antagonist, cardio protective, anti-ischemic, anticancer, anti-HIV, non-peptide thrombin receptor antagonist, and tumor necrosis factor-α antagonist activities. However, the 2-imino derivatives of thiazolidinones are explored to a lesser extent. Several methods are reported in literature for the preparation of thiazolidinone derivatives. Our aim of this research is the "Synthesis of Novel Iminothaizolidinones Derivatives , Characterization and its Biological Activities"

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Methodology to be adopted:

The following are the method which is to be adopted for the proposed research work. Each and every method having its peculiarities and advantages over the conventional methods:-

1. Synthesis of Different Fluorinated Anilines.

2. Synthesis of targeted Iminothiazolidinone Scaffold.

3. Characterization and NMR studies for determination of stereochemistry of Imine and Olefin bond.

4. Study of different methodology for synthesis.

5. Evaluated them for antimicrobial land anti-inflammatory activities and structure activity relationship.

Importance of study/ Society application:

2 International status:

This type compounds containing Iminothiazolidinones have not been used at international levels by others for antibacterial, anti-inflammatory screening. Synthesis of various biological active molecules having Iminothiazolidinones moiety has been subject of many laboratories across the globe

2 National status:

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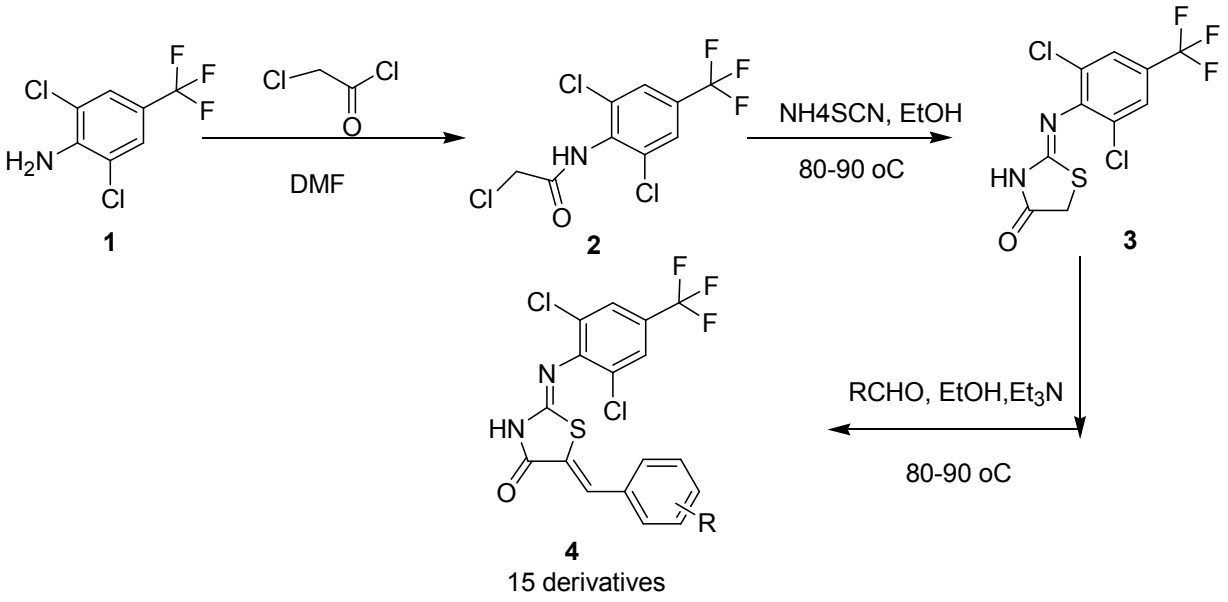
3. **Significance of the study**

Compounds synthesize in this study are Potential antibacterial and anti-inflammatory, anti-diabetic and anticancer agents after primary evaluation can be further patented and use for further study.

Proposed Scheme I:

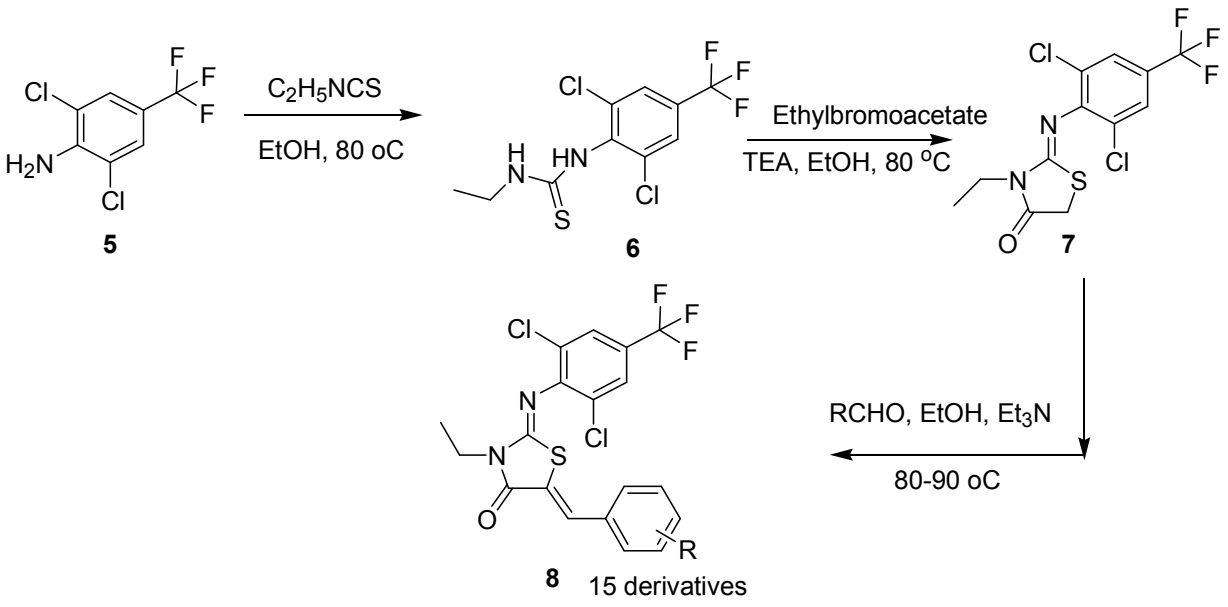
Synthesis of Iminothiazolidinone (**compound 3**) and its different benzilidine derivatives (**compound 4**) are prepared in ethanol using Knovengel reaction. We have also planned NMR studies of compound **3** and **4** for determination of stereochemistry across Olefin bond as there are chances of formation of E & Z stereoisomer's.



Scheme 1

Proposed Scheme II:

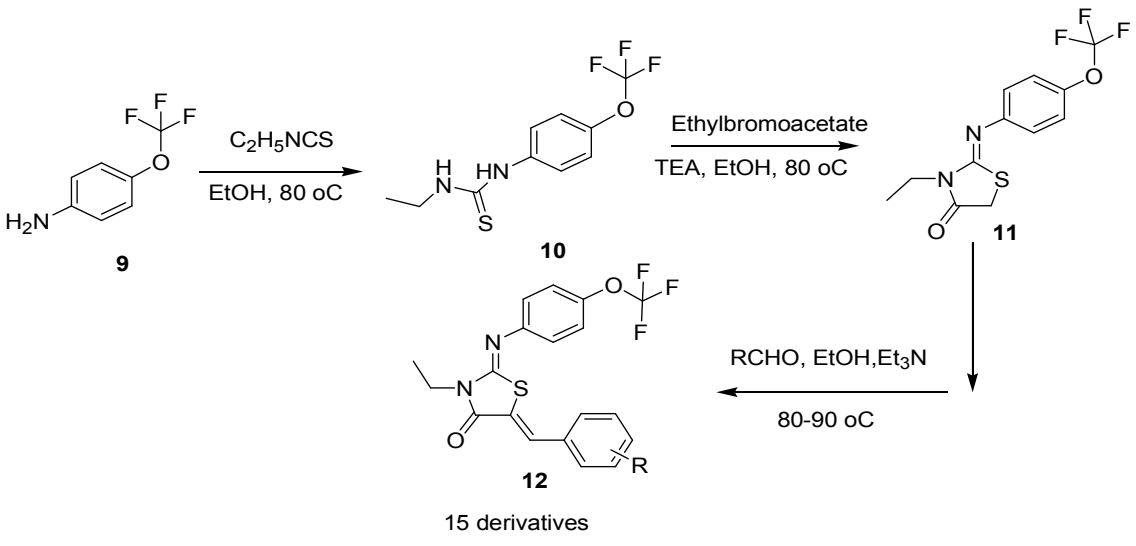
In this Synthesis we will mask the free NH of Iminothiazolidinone ring (**compound 7**) and its different benzilidine derivatives (**compound 8**) are prepared in ethanol using Knovengel reaction. We have also planned NMR studies of compound 3 and 4 for determination of stereochemistry across Olefin bond as there are chances of formation of E & Z stereoisomer's. We have also planned and different methodology for synthesis to control stereochemistry.



Scheme 2

Proposed Scheme III:

We will use different trifluorosubstituted anilines to synthesize target **compound 12** and other trifluorinated derivative using different stating material to find out structure activity relationship.



Scheme 3

Proposed Work Plan:

Year wise plan of work and targets to be achieved

First Year:

- Synthesis of Different Substituted anilines.
- Molecular Modeling Study of Targeted compounds.
- Synthesis of Different type iminothiazolidinones.

Second year:

- Characterization and NMR studies for determination of Stereochemistry across Imine and Olefin.
- Synthesis of Different type iminothiazolidinones derivatives.

Third Year:

- Study of different methodology for synthesis of Iminothiazolidinones using Green Synthesis approach, alternative Base, route
- Evaluated them for antimicrobial land anti-inflammatory activities
- Research paper writing. Thesis writing and Submission

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